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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,874	04/19/2005	Ryuji Ueno	Q87423	5640

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EXAMINER	
POLANSKY, GREGG	
ART UNIT	PAPER NUMBER
1614	
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03/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,874	UENO, RYUJI	
	Examiner	Art Unit	
	GREGG POLANSKY	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-13 and 18-21* is/are pending in the application.

4a) Of the above claim(s) *3,4,6,8,10 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7,9,11-13 and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/09/2008 has been entered.

2. Applicant's response, filed 12/09/2008, to the Advisory Action mailed 11/12/2008 is acknowledged. Amendments of the claims, filed 10/09/2008 and denied entry, are hereby entered as incorporated in the presently submitted claims. Applicant has amended Claims 1, 3, 4, 6, 8, and 10, canceled Claims 16 and 17, added Claims 18-21, and presented arguments.

3. Claims 1, 3-13, and 18-21 are pending.

4. New Claim 18 does not read on the elected specie. Therefore, Claim 18 and dependent Claims 3, 4, 6, 8, and 10 are withdrawn from consideration as they are not drawn to the elected specie.

5. Claims 1, 5, 7, 9, 11-13, and 19-21 are presently under consideration.

6. The scope of the search has been broadened to include 13,14-dihydro-15-keto-16,16-difluoro-PGE_2.

7. Applicant's arguments have been fully considered and are persuasive in part. Rejections and/or objections not reiterated from previous office actions are hereby

withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Oath/Declaration

8. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The provisional application for which Applicant is claiming priority is misnumbered.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 20 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claims 20 and 21, the phrase **"general** formula" (emphasis added) renders the claim indefinite because the claims limit the compounds by way of limiting what constituents are included, thus conflicting with the word "general" in the phrase.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1, 5, 7, 9, 11-13, and 19-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

Claim 1 has been amended to include the limitation "administering to a mammalian subject in need of reduction of body weight". The Specification as originally filed fails to provide support for this new claim limitation. Similarly, newly added Claim 20, which depends from Claim 1, includes the limitation of administration of an effective amount of a prostaglandin compound represented by formula (I) "to reduce body weight", and new Claim 21 is directed to "[a] method for reducing body weight". The Specification as originally filed fails to provide support for these new claims.

Applicant asserts the last paragraph on page 26 of the Specification provides support for these new claim limitations.

The Examiner does not agree with Applicant's assertion. The last paragraph on page 26 merely describes exemplary data depicted in Fig. 1, stating "Fig.1 shows the changes of body weight from the pre-values in each group at **3** weeks after the initiation of the administration [of 13,14-dihydro-15-keto-16,16-difluoro-PGE_1]. As shown in Fig.1, body weight reductions were observed in all test groups while an increase was

observed in the control group. The body weight of the test groups decreased in a dose dependent manner." No statistical analysis of the data is provided. The Specification does not indicate whether the test subjects were obese and in need of a reduction of body weight. Thus, the data presented in Fig. 1 provides a teaching of an apparent reduction of body weight in human test subject of undisclosed weight status, at doses of 24, 48 and 72 µg of 13,14-dihydro-15-keto-16,16-difluoro-PGE_1. However, the present claims are much broader than the teaching of Fig. 1. The Specification fails to provide support for the full breadth of the claims as amended and newly added. Therefore, the claims are properly rejected under 35 U.S.C. 112, 1st paragraph for containing new matter.

13. Claims 1, 5, 7, 9, 11-13, and 19-21 are rejected under 35 U.S.C. 112, first paragraph, because the Specification, while being enabling for reducing the weight of obese patients, does not reasonably provide enablement for the prevention of obesity. The Specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. This is a Scope of Enablement rejection.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior

art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The instant claims are drawn to a method for treating obesity or reducing body weight in a mammalian subject in need of treatment for obesity by administering an effective amount of prostaglandin compounds defined by formula (I) of the claims. The number of compounds defined by formula (I) is large. The Specification defines the term "treatment" to include "any means of control such as prevention, care, relief of the condition, attenuation of the condition and arrest of progression". See page 24, lines 20-22. The claims are very broad since they encompass the prevention of abnormal body weight gain of any etiology.

(3) The state of the prior art:

The Merck Manual teaches that people are considered to be overweight when their body mass index (BMI) is over 25; a person with BMI of 30 or more is considered to be obese. See page 1, 1st 5 lines. The Merck Manual teaches that obesity "results from consuming more calories than the body uses". There are many factors that influence weight gain, including: genetic and environmental factors, physical inactivity, alcohol consumption, socioeconomics, menopause in women, stress, polycystic ovary syndrome, pharmaceuticals, and smoking cessation. See page 2.

(4) The predictability or unpredictability of the art and (5) the relative skill of those in the art:

The relative skill of those in the art of pharmacology and medicine and the unpredictability of the pharmacological and biological arts are very high. In fact, the courts have made a distinction between mechanical elements, which function the same in different circumstances, yielding predictable results, and chemical and biological compounds, which often react unpredictably under different circumstances. *Nationwide Chem. Corp. v. Wright*, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); *In re Fischer*, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. Likewise, the physiological or pharmaceutical activity of preventing obesity, particularly with regard to the multitude of factors which influence the development of obesity, is an unpredictable art.

Thus, it is not understood how one skilled in the art can reasonably expect that the instant compound can be administered in order to have the "preventive" effect.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The Specification has provided guidance and a working example for a method of reducing body weight in humans by the oral administration of a single prostaglandin compound (the elected 15-keto PGE_1 compound), at doses of 24, 48, and 72 μg/day. See pages 25 and 26. The Specification does not disclose whether the test subjects were obese. It is noted that the disclosure does not provide any evaluation of the statistical evaluation of the significance of the results.

(8) The quantity of experimentation necessary:

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. *In re Fisher*, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. *In re Fisher*, 427 F.2d 839, 166 USPQ 24; *Ex Parte Hitzeman*, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. *In re Wright*, 999 F.2d 1562-63, 27 USPQ2d 1575. The Office maintains a very high standard of enablement for claims drawn to methods of prevention. As discussed above, considering above factors, especially the "sufficient working examples", "the level of skill in the art", "the relative skill and the unpredictability in the pharmaceutical art", "breadth of the claims" and "the chemical nature of the invention", one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the claimed compounds for the claimed methods of prevention.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 1, 5, 7, 9, 12, 13, and 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Ueno et al. (U.S. Patent No. 5,234,954).

Ueno et al. teach a method for the treatment of hyperlipidemia comprising administration of a 15-keto-prostaglandin compound, including a 13,14-dihydro-15-keto-16,16-difluoro-prostaglandin E compound. See Abstract; column 15, "FORMULATION EXAMPLE 2"; column 20, claim 6; and column 22, claim 10. Ueno et al. teach both the PGE1 and PGE2 forms of the 15-keto prostaglandin compounds are useful in the disclosed methods. See last paragraph bridging columns 3-4. Ueno et al. teach the disclosed PGE compounds decrease blood levels of triglyceride, cholesterol or phospholipid (irrespective of cause, e.g., disease, drug or food) by promoting release into the intestine or release with feces. Further, Ueno et al. teach the method useful for reducing said blood lipids in obese individuals. See column 15, lines 27-45. The reference teaches the PGE compounds may be administered systemically by known methods of administration and "the dosage will vary depending on the particular animal or human patient, age, body weight, symptom to be treated, desired therapeutic effect, administration route, term of treatment and the like, [and] satisfactory effects will be obtained with the dosage of 0.001-500 mg/kg administered in 2 to 4 divided doses a day or as a sustained form". See column 14, lines 20-31. With respect to claimed dosage ranges of the active agents in the instant methods, it is not inventive to discover the optimum or workable ranges by routine experimentation when general conditions of a

claim are disclosed in the prior art. See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233,235 (CCPA 1955) and MPEP 2144.05(11).

Treating hyperlipidemia in obese individuals with the same PGE compounds at the same doses as instantly claimed, as disclosed by Ueno et al., would naturally produce the same reduction of body weight as is instantly claimed. It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicant to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention"). Also see *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1343-44, 74 USPQ2d 1398, 1406-07 (Fed. Cir. 2005) (holding that a prior art patent to an anhydrous form of a compound "inherently" anticipated the claimed hemihydrate form of the compound because practicing the process in the prior art to manufacture the

anhydrous compound "inherently results in at least trace amounts of" the claimed hemihydrate even if the prior art did not discuss or recognize the hemihydrate).

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 1, 5, 7, 9, 11, 12, 13, and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ueno et al. (U.S. Patent No. 5,234,954), as evidenced by Dietz (Pediatrics, Vol. 101, Issue 3 (Supplement), pages 518-525).

The teachings of Ueno et al. are presented *supra*.

Hyperlipidemia is common in obese individuals. See Dietz, page 518 "Abstract" and page 521, "Hyperlipidemia". It would have been obvious to one of ordinary skill in the art at the time of the invention to utilize the teachings of Ueno et al. to treat a common symptom of obesity, hyperlipidemia, by the administration of a 15-keto-prostaglandin compound, including a 13,14-dihydro-15-deto-16,16-difluoro-prostaglandin E compound (*supra*). One would have been motivated to do so by the teaching of Ueno et al. (i.e., 15-keto-prostaglandin compounds are useful for reducing blood lipids in obese individuals) with further motivation provided by Dietz (i.e., hyperlipidemia association with obesity).

As was noted *supra*, Ueno et al. teach both the PGE1 and PGE2 forms of the 15-keto prostaglandin compounds are useful in the disclosed methods. However, they do not specifically disclose the PGE1 for of the instantly elected 15-keto prostaglandin (they disclose the PGE2 form). It would have been obvious to one of ordinary skill in the art to also evaluate the effectiveness of PGE1 form of the 15-keto prostaglandins, since Ueno et al. teach both forms of the 15-keto prostaglandins useful.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

18. Claims 1, 5, 7, 9, 11, 12, 13, and 19-21 are rejected.

19. No claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GREGG POLANSKY whose telephone number is

(571)272-9070. The examiner can normally be reached on Mon-Thur 9:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregg Polansky/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614